Propofol Exhibits Inhibitory Effect Towards Human Liver Microsomes (HLMs)- Catalyzed Glucuronidation of Thienorphine

Shu-Yao ZHANG 1#, Lei CHEN 2#, Chao-Xian LIN 3,*, Zhi-Wei ZHU 1, Ling FANG 1, Dai-Shan XIN 1, & Dai-Nian GUO 3

1 Intravenous drug use deployment center, Cancer Hospital of Medical College, Shantou City, Guangdong Province, 515031, China
2 Shantou University Medical College Cancer Hospital, No. 7, Raoping Road, Shantou, 515041, China
3 Office of the new drug clinical trials, Cancer Hospital of Medical College, Shantou University, Shantou City, Guangdong Province, 515031, China

SUMMARY. Drug-drug interaction (DDI) is a challenging problem in the process of drug utilization. Inhibition of glucuronidation reaction of drugs is a major reason for DDI. The aim of the present study is to predict propofol-thienorphine interaction from the perspective of propofol’s inhibition towards thienorphine glucuronidation. The human liver microsomes (HLMs) incubation system supplemented with uridine 5’-diphosphoglucuronic acid (UDPGA) was used. The results showed that propofol inhibited HLMs-catalyzed thienorphine glucuronidation in a concentration-dependent manner. Both Dixon plot and Lineweaver-Burk plot showed that the inhibition of thienorphine glucuronidation by propofol was best fit to competitive inhibition, and the second plot using slopes from Lineweaver-Burk plot versus thienorphine concentration was used to determine the inhibition kinetic parameter (K_i) value to be 365.9 μM. Whether the in vitro inhibition of propofol towards thienorphine glucuronidation can induce the in vivo propofol-thienorphine interaction might be influenced by many factors, including various pharmacokinetic factors influencing the in vivo concentration of propofol. These data should be carefully explained due to complicated factors influencing the in vitro-in vivo extrapolation (IVIVE) results.

KEY WORDS: Drug-drug interaction (DDI), Propofol, Thienorphine.
* Author to whom correspondence should be addressed. E-mail: linchaoxian123456@163.com; # These two authors equally contributed to this work.